



Aicardi-Goutieres syndrome

Aicardi-Goutieres syndrome is a disorder that mainly affects the brain, the immune system, and the skin.

Most newborns with Aicardi-Goutieres syndrome do not show any signs or symptoms of the disorder at birth. However, about 20 percent are born with a combination of features that include an enlarged liver and spleen (hepatosplenomegaly), elevated blood levels of liver enzymes, a decrease in blood platelets (thrombocytopenia), and abnormal neurological responses. While this combination of signs and symptoms is typically associated with the immune system's response to congenital viral infection, no actual infection is found in these infants. For this reason, Aicardi-Goutieres syndrome is sometimes referred to as a "mimic of congenital infection."

Within the first year of life most individuals with Aicardi-Goutieres syndrome experience an episode of severe brain dysfunction (encephalopathy), typically lasting for several months. During this phase of the disorder, affected babies are usually extremely irritable and do not feed well. They may develop intermittent fevers in the absence of infection (sterile pyrexias) and may have seizures. They stop developing new skills and begin losing skills they had already acquired (developmental regression). Growth of the brain and skull slows down, resulting in an abnormally small head size (microcephaly). In this phase of the disorder, white blood cells and molecules associated with inflammation can be detected in the cerebrospinal fluid, which is the fluid that surrounds the brain and spinal cord (central nervous system). These abnormal findings are consistent with inflammation and tissue damage in the central nervous system.

The encephalopathic phase of Aicardi-Goutieres syndrome leaves behind permanent neurological damage that is usually severe. Medical imaging reveals deterioration of white matter in the brain (leukodystrophy). White matter consists of nerve fibers covered by myelin, which is a substance that insulates and protects nerves. Affected individuals also have abnormal deposits of calcium (calcification) in the brain.

Most people with Aicardi-Goutieres syndrome have profound intellectual disability. They also have significant neuromuscular problems including muscle stiffness (spasticity); involuntary tensing of various muscles (dystonia), especially those in the arms; and weak muscle tone (hypotonia) in the trunk.

About 40 percent of people with Aicardi-Goutieres syndrome have painful, itchy skin lesions, usually on the fingers, toes, and ears. These puffy, red lesions, which are called chilblains, are caused by inflammation of small blood vessels. They may be

brought on or made worse by exposure to cold. Vision problems, joint stiffness, and mouth ulcers may also occur in this disorder.

As a result of the severe neurological problems usually associated with Aicardi-Goutieres syndrome, most people with this disorder do not survive past childhood. However, some affected individuals who have later onset and milder neurological problems may live into adulthood.

Frequency

Aicardi-Goutieres syndrome is a rare disorder. Its exact prevalence is unknown.

Genetic Changes

Mutations in the *TREX1*, *RNASEH2A*, *RNASEH2B*, *RNASEH2C*, and *SAMHD1* genes have been identified in people with Aicardi-Goutieres syndrome.

The *TREX1*, *RNASEH2A*, *RNASEH2B*, and *RNASEH2C* genes provide instructions for making nucleases, which are enzymes that help break up molecules of DNA and its chemical cousin RNA. Mutations in any of these genes are believed to result in an absent or dysfunctional nuclease enzyme. Researchers suggest that absent or impaired enzyme function may result in the accumulation of unneeded DNA and RNA in cells. These DNA and RNA molecules or fragments may be generated during the first stage of protein production (transcription), copying (replication) of cells' genetic material in preparation for cell division, DNA repair, cell death, and other processes. The unneeded DNA and RNA may be mistaken by cells for that of viral invaders, triggering immune system reactions that result in encephalopathy, skin lesions, and other signs and symptoms of Aicardi-Goutieres syndrome.

The *SAMHD1* gene provides instructions for making a protein whose function is not well understood; however, it is believed to be involved in the immune system and the inflammatory process. Mutations in this gene likely result in a protein that does not function properly, resulting in immune system abnormalities, inflammatory damage to the brain and skin, and other characteristics of Aicardi-Goutieres syndrome.

Inheritance Pattern

Aicardi-Goutieres syndrome can have different inheritance patterns. In most cases it is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Rarely, this condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. These cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- AGS
- Aicardi Goutieres syndrome
- Cree encephalitis
- encephalopathy with basal ganglia calcification
- familial infantile encephalopathy with intracranial calcification and chronic cerebrospinal fluid lymphocytosis
- pseudo-TORCH syndrome
- pseudotoxoplasmosis syndrome

Diagnosis & Management

These resources address the diagnosis or management of Aicardi-Goutieres syndrome:

- GeneReview: Aicardi-Goutieres Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1475>
- Genetic Testing Registry: Aicardi Goutieres syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0393591/>
- Genetic Testing Registry: Aicardi Goutieres syndrome 1
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796126/>
- Genetic Testing Registry: Aicardi Goutieres syndrome 2
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3489724/>
- Genetic Testing Registry: Aicardi Goutieres syndrome 3
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835916/>
- Genetic Testing Registry: Aicardi Goutieres syndrome 4
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835912/>
- Genetic Testing Registry: Aicardi Goutieres syndrome 5
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2749659/>

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Leukodystrophies
<https://medlineplus.gov/leukodystrophies.html>

Genetic and Rare Diseases Information Center

- Aicardi-Goutieres syndrome
<https://rarediseases.info.nih.gov/diseases/575/aicardi-goutieres-syndrome>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke (NINDS): Encephalopathy Information Page
<https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page>

Educational Resources

- Centers for Disease Control and Prevention: Intellectual Disability
https://www.cdc.gov/ncbdd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Disease InfoSearch: Aicardi-Goutieres Syndrome
<http://www.diseaseinfosearch.org/Aicardi-Goutieres+Syndrome/275>
- Malacards: aicardi-goutieres syndrome
http://www.malacards.org/card/aicardi_goutieres_syndrome
- Orphanet: Aicardi-Goutieres syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=51

Patient Support and Advocacy Resources

- International Aicardi-Goutieres Syndrome Association
<http://www.aicardi-goutieres.org/index.jsp?lingua=ENG>

GeneReviews

- Aicardi-Goutieres Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1475>

Genetic Testing Registry

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<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796126/>
- Aicardi Goutieres syndrome 2
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C3489724/>
- Aicardi Goutieres syndrome 3
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835916/>
- Aicardi Goutieres syndrome 4
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835912/>
- Aicardi Goutieres syndrome 5
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2749659/>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Aicardi-Goutieres+syndrome%22>

Scientific articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28aicardi-goutieres+syndrome%5BTIA%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

OMIM

- AICARDI-GOUTIERES SYNDROME 1
<http://omim.org/entry/225750>
- AICARDI-GOUTIERES SYNDROME 2
<http://omim.org/entry/610181>
- AICARDI-GOUTIERES SYNDROME 3
<http://omim.org/entry/610329>
- AICARDI-GOUTIERES SYNDROME 4
<http://omim.org/entry/610333>
- AICARDI-GOUTIERES SYNDROME 5
<http://omim.org/entry/612952>

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